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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/802,110 | 03/07/2001 | James Leushner | VGEN.P-058-2 | 5580 |
| 26582 | 7590 | 08/29/2005 | EXAMINER | |
| HOLLAND & HART, LLP 555 17TH STREET, SUITE 3200 DENVER, CO 80201 | | | WILDER, CYNTHIA B | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1637 | |
| DATE MAILED: 08/29/2005 | | | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

09/802,110

Applicant(s)

LEUSHNER ET AL.

Examiner

Cynthia B. Wilder, Ph.D.

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 13-36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 13-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's amendment filed June 6, 2005 is acknowledged and has been entered. Claim 1 has been amended. All of the arguments have been thoroughly reviewed and considered but are not found persuasive in view of the new grounds of rejections necessitated by Applicant's amendment of the claims. Any rejection not reiterated in this action has been withdrawn as being obviated by the amendment of the claims.

This action is made FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Previous rejections

3. The claim rejection under 35 USC 112 second paragraph is withdrawn in view of Applicant's amendment. The prior art rejections under 35 USC 103(a) directed to claims 13 and 25 are withdrawn in view of the new grounds of rejections

Claim Rejections - 35 USC § 103

New Ground(s) of Rejections

THE NEW GROUND(S) OF REJECTIONS WERE NECESSITATED BY APPLICANT'S AMENDMENT OF THE CLAIMS:

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

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patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 13-16 and 25-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Jordan (US 6017699, filing date (March 1996)). Jordan teaches a kit consisting of, in package combination, a single reaction vessel (microtitre plate) for each DNA region to be sequenced containing a mixture of region-specific reagents sufficient for sequencing the sense and anti-sense strand of each DNA region of a genomic DNA sample of a microorganism (col. 6, lines 55 to col. 7, line 4), wherein the region-specific reagents comprises a pair of primers which binds to the sense (coding) and antisense (noncoding) strands (col. 10, lines 7-17). The reference^{es} do not expressly state that the primers flank the target DNA regions within the genomic microorganism's DNA. However, this is deemed inherent in the teaching of the construction of the set of species-specific primers for PCR amplification (col. 5, lines 7-17 and Example 4 in it's entirety). Likewise it is commonly known in the art that in PCR amplification reactions, primers that bind to the sense and antisense strands of the target DNA sample also flank the target region to be amplified. Therefore, Jordan meets the limitations of claims 13-16 and 25-28.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 13, 17-25 and 29-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mathies et al (Us 5,707,804, filing date March 1995) and Ruano (5,427,911, (patent date June 27, 1995) in view of Rao (Analytical Biochemistry, vol. 216, pages 1-14, (1994) and further in view of Ahern (The Scientist, Vol. 9, No. 15, pages 1-15, June 1995). Regarding claims 13, 17-25 and 29-36, Mathies et al teach a method and kit for sequencing nucleic acid, the method comprising primer pairs for copying a single stranded nucleic acid and dideoxynucleotide for terminating the chain at a particular nucleotide , the mixture further comprising a DNA polymerase, dNTPS and separate reaction vessels to generate the single stranded DNA fragments (col. 10, lines 26-62 and col. 14, lines 12-26). Mathies et al do not teach wherein all of the sequencing reagents are in the form of a kit.

Ruano et al. teach a method for sequencing genomic DNA sample, the method comprising amplifying in vitro with two locus specific primers that flank both ends of the target region to obtain a template, synthesizing simultaneously truncated strands from both ends of the template by introducing a dideoxynucleotide terminator for each of the four bases adenine, guanine, cytosine and thymine and introducing a label or labels specific for either or both of the 5' ends of the synthesizing strands, thermally cycling steps to provide a sufficiently readable signal (col. 2,

lines 3-23). Ruano further teaches wherein the dideoxynucleotide triphosphate is in a mole ratio of about 1:10 to the corresponding deoxynucleotide triphosphate (col. 6, lines 47-68).

The reference of Ruano differs from the instant invention in that the reference does not teach wherein the method comprises the dideoxynucleotide triphosphate in a mole ratio of 1:50 to 1: 1000 or in a mole ratio of 1:1000 to 1: 500 to the corresponding deoxynucleotide triphosphates.

In a method similar to that of Ruano, Rao teaches a method of direct sequencing of polymerase chain reaction-amplified DNA. Rao teaches wherein the method comprises mixing the PCR-amplified genomic DNA, labeled primer sequencing buffer and Taq polymerase in a tube, adding to the mixture in four separate tubes, four dNTPs and at least one dideoxynucleotide triphosphate, perform thermal cycling (see Table 3, page 5). Rao differs from the instant invention in that Rao does not teach wherein the mole ratio of the ddNTP:dNTP is from 1:50 to 1:1000 or 1:100 to 1:500. Rao also does not teach wherein the polymerase enzyme incorporates dNTPs into an extending nucleic acid polymerase at a rate which is no less than 0.5 times the rate of incorporation of dNTPs. However, Rao discloses that the composition of the dNTP/ddNTP mix varies depending on the type of polymerase preparation used. Rao additionally states that different polymerases require different dNTP/ddNTP ratios for optimal chain terminations and therefore, the reagents or kits for one polymerase cannot be substituted with those for a different polymerase. Rao further teaches that optimal buffer conditions for the synthesizing reaction will vary based on the specific DNA polymerase used (see Table 3 legend).

In a review article Ahern teaches the advantages of a kit. Ahern teaches that a kit provides convenience, time management and ease of practicing to the investigator (page 4, second-fourth paragraphs). Therefore in view of the foregoing, one of ordinary skill in the art at the time of the claimed invention would have recognized that the mole ratio of reagents of the kit and polymerase extending ability may vary based on the chose of polymerase preparation used in

the sequencing reaction and desired results as suggested by Rao. One of ordinary skill in the art at the time of the claimed invention would have been further motivated to have combined the components of the sequencing method as taught by Ruano and Rao in the form of a kit for the obvious benefits taught by Ahern that a kit provides convenience, time management and ease of practicing to the investigator.

Conclusion

8. No claims are allowed. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia B. Wilder, Ph.D. whose telephone number is (571) 272-

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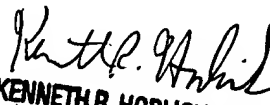
0791. The examiner works a flexible schedule and can be reached by phone and voice mail. Alternatively, a request for a return telephone call may be emailed to cynthia.wilder@uspto.gov. Since email communications may not be secure, it is suggested that information in such request be limited to name, phone number, and the best time to return the call.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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KENNETH R. HORLICK, PH.D.
PRIMARY EXAMINER

8/22/05